REMARKS

Claims 21-26 are pending in the application. Claims 21-26 are rejected. Claims 22-24 are amended herein to correct claim dependencies. The title has been amended that is clearly indicative of the invention to which the claims are directed.

Claim Objections

The Examiner objects to Claim 24 as an "essential duplicate of claim 1". Applicants respectfully point out that Claim 1 was cancelled in the Preliminary Amendment filed on December 12, 2003. Moreover, amended Claim 24 is distinguished over Claim 21 in that Claim 21 uses the transitional phrase "comprising" whereas Claim 24 (dependent on Claim 21) uses the phrase "consisting of".

Claim Rejections – 35 U.S.C. §112

Claims 22, 23 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for recitation of "bulk of antigen". Applicants traverse and respectfully assert that "bulk antigen" and similar phrases, including "bulk of antigen" are terms of art that are easily understood by those of skill in this art. These terms refer to the bulk of antigen preparations used in the manufacture of vaccines; i.e., a large quantity of antigen preparation that is normally separated into separate doses (cf. Webster's Ninth New Collegiate Dictionary, 1989 definition of "bulk" used as the phrase "in bulk": not divided into parts or packaged in separate units). Moreover, an Internet search using the Google search engine returned multiple instances of the term "bulk antigen" referring to large preparations of antigens for use in formulating vaccine doses. Accordingly, the use of the term "bulk of antigen" in claims 22, 23 and 25-26 is not indefinite to one of skill in this art.

Claim Rejections – 35 U.S.C. §§102 and 103

Claims 21-26 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Whittle et al. (WO 96/26277). Applicants traverse and respectfully assert that Whittle et al. does not disclose or suggest the instantly claimed invention. Whittle et al. is concerned with vaccines against HPV that comprise polypeptide aggregates. In fact, all of Whittle's examples and the bulk of

his detailed description concern fusion proteins, and in particular a fusion of the L2 and E7 proteins of HPV. Whittle's aggregates are the result of the formation of L2E7 inclusion bodies in *E. coli*, and in some cases solubilization and reaggregation of these proteins. Whittle does not disclose or suggest the use of HPV VLPs comprising L1, and in fact teaches away from using such moieties in his vaccines. At page 7, lines 18-20, Whittle states that the "aggregated soluble or disperse products" of his invention "are otherwise distinct from virus-like particles based on papillomavirus L1 protein". Whittle specifically excludes HPV VLPs from the scope of his invention. Accordingly, the instant claims, limited to HPV proteins in the form of VLPs, are not anticipated or obvious in view of Whittle et al.

Claims 21-26 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Bruck et al. (WO 99/10375). Applicants traverse. The invention described by Bruck et al. is an HPV E6, E7 or E6/E7 polypeptide fused to an immunological fusion partner. As part of Bruck's disclosure, she suggests that pharmaceutical compositions comprising the inventive fusion proteins may also contain other HPV proteins, including VLPs from HPV 16 or HPV 18. Bruck et al. does not disclose compositions comprising VLPs from HPV 16 and HPV 18, and certainly does not describe or suggest vaccine compositions that consist of HPV 16 VLPs and HPV 18 VLPs (see instant Claim 24). In addition, there is no disclosure in Bruck et al. of the absorption of VLPs onto an aluminum salt. Accordingly, Bruck et al. does not disclose each and every element of the instant invention and therefore does not anticipate the instant claims.

Claims 21-26 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Whittle et al. (US Patent No. 6,123,948). The specification of US 6,123,948 is essentially identical to Whittle et al. (WO 96/26277) discussed above. In particular, at column 5, lines 41-50, Whittle again does not disclose or suggest the use of HPV VLPs comprising L1, and in fact teaches away from using such moieties in his vaccines. Thus, for same reasons as those discussed for WO 96/26277, the instant claims are not anticipated or obvious in view of US 6,123,948.

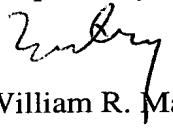
Claims 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volkin et al. (US Patent No. 6,251,678 B1), and Thompson et al. (Biochemical Society Transactions, 1997, 274S). Applicants traverse and respectfully assert that there is no motivation to combine the cited references to reach the instant claims. Volkin et al. is

concerned with formulations that stabilize HPV VLPs (either in solution or absorbed onto aluminum adjuvant particles) during long term storage. Volkin does not mention any other HPV proteins, nor is there any discussion of any other adjuvant or the reasons for inclusion of any particular adjuvant. However, it was known to the skilled artisan that aluminum adjuvants are favored for induction of humoral (TH2) immune responses. Moreover, it was expected that an immunoprophylactic response targeted to a surface antigen such as the L1 protein of HPV would be primarily humoral in nature. Hence, Volkin et al.'s choice of aluminum as an adjuvant was logical. In contrast, Thompson et al. describe a means for treatment of an existing condition (genital warts caused by HPV 6 and 11 infection) by administration of a therapeutic vaccine. Moreover, Thompson et al. make clear that their goal is to preferentially enhance T cell (TH1) immune responses, again a sensible goal in view of the immunogen that they disclose (a fusion protein comprising an early antigen of HPV thought to be an appropriate target a cell mediated immune response). Accordingly, Thompson et al. suggest to one skilled in this art the use of MPL to preferentially stimulate cellular (TH1) immunity.

There is thus no motivation to combine Volkin et al. (vaccines comprising HPV VLPs, a TH2-type immunogen, and a TH2 adjuvant (aluminum)) with Thompson (vaccines comprising HPV E7, a TH1-type immunogen, and a TH1 adjuvant (MPL)) to reach the instant invention (VLPs, TH2-type immunogens, a TH2 adjuvant (aluminum), and a TH1 adjuvant (MPL)). That is, there is no motivation or suggestion in either reference to utilize a TH1 adjuvant like MPL with an HPV VLP (a TH2 immunogen) either alone or in combination with an aluminum adjuvant.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the subject application is in condition for allowance. If the Examiner has any remaining objections or concerns, the Examiner is respectfully requested to contact Applicants' undersigned attorney to resolve such issues and advance the case to issue.

Respectfully submitted,



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